

purpose of updating the best mode, and does not introduce new matter into the specification. The composition of the solution itself remains unchanged and is described generically in the specification.

In the Office Action dated September 14, 1995, issued in the parent case of the present divisional application, Application No. 08/395,113, now issued as U.S. Patent No. 5,556,379, dated September 17, 1996, pending claims 59-66 were rejected under 35 U.S.C. § 103, as being obvious.

I. *At page 2 of the Office Action issued in the parent application, the Examiner states that claims 59-66 were rejected under 35 U.S.C. § 103, as being unpatentable over Draenert '282 in view of Helenius.*

The Examiner states that Draenert discloses a process for cleaning bone comprising the steps of selecting a bone and applying a vacuum to the bone in order to remove bone marrow. The Examiner points to column 2, lines 9-12. The Examiner admits that Draenert does not disclose the use of a solution to solubilize the bone marrow. The Examiner contends that Helenius discloses the use of various detergent solutions for cleaning bone. The Examiner concludes that it would have been obvious to one having ordinary skill in the art at the time the invention was made to include the detergents disclosed in Helenius in the invention disclosed in Draenert in order to clean bone.

A brief analysis of Draenert and Helenius is set forth below.

Draenert is directed to a suction drainage bone screw which enables the spongiosa honeycombs of living bone to be filled with bone cement during arthroplastic surgery without endangering the life of the patient. Draenert discloses a process for ensuring that bone cement can penetrate into the honeycombs of the bone marrow matrix of *living* bone when an implant is inserted into the bony bed. In order to ensure that the bone cement can penetrate into the honeycombs, Draenert states that fat, marrow and cellular components are removed in order to create a partial vacuum in the bone. Draenert inserts the bone screw into the bone of a living patient and removes fat, marrow and cellular components under vacuum to create a partial vacuum in the bone, which partial vacuum aids in drawing bone cement into the honeycombs to firmly anchor the implant into the bony bed.

Example 1 states that a cannulated bone screw is anterolaterally inserted into the femur beneath the sight which corresponds to the tip of the implanted metal prosthesis. The process of evacuation is carried out via the longitudinal canal of the bone screw with the result that a vacuum builds up in the bone. Thereafter, the femur is proximally sealed with silicone rubber and the bone cement applied from the proximal direction to the distal direction followed by the insertion of a plastic replica of a meller standard prosthesis. Example 1 also states that the results of using the distal application of vacuum leads to a water-tight bone cement filling from the region of the shaft up to the transition of the metaphysis.

Helenius discloses various detergents and their properties including the effects of detergents on biological membranes, solubilization of lipid layers, etc. In view of the following, this rejection is respectfully traversed.

**II. Regarding the Examiner's contention, it is submitted that claims 59-66 are unobvious and patentable under 35 U.S.C. § 103, over Draenert et al. in view of Helenius.**

- 1. Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness.**
  - a. Draenert is not analogous art; therefore Draenert cannot be combined with other references to determine the patentability of the present claims.**

Applicant submits that Draenert is non-analogous prior art and is thus not relevant in determining obviousness. It is noted that the Court in *In re Clay*, 966 F.2d 656, 23 USPQ.2d 1058 (Fed. Cir. 1992) held that the PTO committed clear error in finding a cited reference to be analogous art which could be combined with other references to determine the patentability of Applicant's claims. The inventor's field of endeavor in *In re Clay* was storage of refined liquid hydrocarbons. The field of endeavor of the invention of the reference in question was the extraction of crude petroleum, both relating to the petroleum industry. The Court in making its determination as to analogous art applied a two part test for determining whether prior art is analogous: (1) whether the art is from the same field of endeavor, regardless of the problem addressed; and (2) if the reference is not within the field of the inventor's endeavor whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved.

The Court held that the cited reference was not in the inventor's field of endeavor. The Court stated that the reference could not be considered within the inventor's field of endeavor merely because both relate to the petroleum industry. The Court stated that the reference teaches the use of a gel in unconfined and irregular volumes within generally underground natural oil bearing formations to channel flow in a desired direction; the inventor teaches the introduction of gel to a confined dead volume of a man-made storage tank. The Court noted that the reference process operates in extreme conditions, with petroleum formation temperatures as high as 115°C and that significant well bore pressures; the inventor's process operates at ambient temperature and atmosphere pressure. The Court concluded that the inventor's field of endeavor is the storage of refined liquid hydrocarbons while the field of endeavor of the reference invention, on the other hand, is the extraction of crude petroleum.

With regard to the second prong of the test, the Court concluded that the cited reference was not reasonably pertinent to the inventor's problem. The Court stated that a reference is reasonably pertinent if, even though it may be in a different field from the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to the inventor's contention in considering its problem. The Court stated that thus, the purpose of both the invention and the prior art are important in determining whether the reference is reasonably pertinent to the problem the invention attempts to solve. The Court states that if a reference disclosure has the same purpose as the claimed invention, the reference relates to the same problem, and that fact supports use of that reference in an obviousness rejection. An inventor may well have

been motivated to consider the reference when making his invention. If it is directed to a different purpose, the inventor would accordingly have had less motivation or occasion to consider it. The Court concluded that a person having ordinary skill in the art would not have reasonably expected to solve the problem of dead volume in tanks for storing refined petroleum by considering a reference dealing with plugging underground formation anomalies.

The Court stated that the reference is concerned with plugging underground formation anomalies so that fluid is subsequently diverted by the gel into the formation matrix, thereby forcing bypassed oil contained in the matrix toward a production well. The reference is faced with the problem of recovering oil from rock, *i.e.*, from a matrix which is porous, permeable, sedimentary rock of a subterranean formation where water has channeled through formation anomalies and bypassed oil present in the matrix. Such a problem is not reasonably pertinent to the particular problem with which the inventor was involved -- preventing loss of stored product to tank dead volume while preventing contamination of such a product. The Court concluded that the subterranean formation of the reference is not structurally similar to, does not operate under the same temperature as, and does not function like the inventor's storage tanks.

Draenert is directed to a bone screw for use during arthroscopic surgery in a living patient. The bone screw allows bone marrow elements to be drained from the bone matrix in order to create a partial vacuum in the bone, which partial vacuum aids in drawing bone cement into the bone matrix to firmly secure the prosthesis into the bony

bed during arthroplastic surgery. Draenert discloses that the benefit of using the particular bone screw and method is that it is possible to fill the honeycombs with bone cement without endangering the life of the patient. In the present case both Draenert and the present invention are concerned with bone. However, Draenert is not from the same field of endeavor as the present invention. Here, as in *In re Clay*, Draenert cannot be considered in the present inventor's field of endeavor merely because Draenert and the present invention relate to bone. Draenert teaches the use of a bone screw in a living bone in order to create a partial vacuum within the bone to insure that bone cement is adequately drawn into the honeycombs of the bone to firmly anchor the prosthesis into the bone during arthroplastic surgery without endangering the life of the patient. Draenert's process and device operate and are used with a living human during surgery. The present inventor's process operates and is used on cadaveric bone in a laboratory setting. Draenert's field of endeavor is medical devices and surgical methods for use in an *in-vivo* surgical setting, during surgery on a living patient, to prolong the life of the patient. Applicant's field of endeavor is an *in-vitro* method for cleaning cadaveric bone to produce bone matrix free from any bone marrow elements including lipid, blood cells, etc., such bone matrix being suitable for transplantation into a living human at a later time.

Draenert is also not reasonably pertinent to Applicant's problem because the purpose of the present invention and Draenert are different. Again, Draenert is concerned with removing an amount of bone marrow elements from the bone matrix in order to create a partial vacuum within the bone which partial vacuum aids in drawing bone cement into the bone matrix to ensure that the prosthesis is firmly anchored into the

bony bed. Draenert is faced with the problem of anchoring a prosthesis into the bony bed of a bone during arthroscopic surgery, as firmly as possible, without endangering the life of the patient. This problem is not reasonably pertinent to the particular problems with which Applicant is involved, that is, providing an *in-vitro* method for cleaning cadaveric bone to produce bone matrix substantially free from bone marrow elements, which cleaned bone matrix is suitable for eventual transplant into a human. The method of Draenert is not similar to the method of the present invention; the methods are not used under similar conditions, Draenert's method is for use in a living human patient, while the present method cannot be used on a living patient and indeed if used on a living patient would result in the death of the patient. Rather, the present method, is used in an *in-vitro* system. That is, cadaveric bone is cleaned of bone marrow elements to produce a substantially cell-free bone matrix. Lastly, Draenert's method does not function like Applicant's method. Draenert's method uses a vacuum to drain bone marrow elements from the bone to create a partial vacuum in the bone. This partial vacuum is then used to deliver substances including, for example, bone cement to the bone matrix. The present invention requires the solubilization of bone marrow elements by subjecting the matrix of the bone to a negative pressure-mediated flow of solvent. There is no partial vacuum created in the cadaveric bone in the present method. Rather, the bone marrow is solubilized during the negative pressure-mediated flow of solvent and removed via this negative pressure-mediated flow.

In view of the above, it is submitted that Draenert does not constitute analogous art and thus cannot be combined with other references to determine the patentability of Applicant's claims.

b. *Assuming arguendo, Draenert is analogous art, Applicant submits that the combination of Draenert with Helenius is improper since neither Draenert nor Helenius provide any motivation, suggestion or incentive supporting the combination.*

It is noted that the court in *In re Jones*, 958 F.2d 347, 21 USPQ.2d 1941 (Fed. Cir. 1992), held that: "Before the PTO may combine the disclosures of two or more prior art references in order to establish *prima facie* obviousness, there must be some suggestion for doing so,..." Likewise, the court in *In re Bond*, 910 F.2d 831, 15 USPQ.2d 1566 (Fed. Cir. 1990) held that the PTO erred in rejecting the claimed invention as an obvious combination of two prior art reference teachings when the prior art provided no teaching, suggestion or incentive supporting the combination. Lastly, it is noted that the court in *In re Levitt*, 11 USPQ.2d 1315, 1316 (Fed. Cir. 1989), held that: "The mere fact that both references originate from the herbicide art does not provide any teaching or suggestion to combine them. Nor does the fact that both references concern compounds containing a specific ring suggesting that substituents suitable in one case would be expected to be suitable in the other."

Draenert is directed to an *in-vivo* surgical process to ensure optimal anchoring of an implant during arthroplastic surgery by bone cement, while Helenius is concerned with the solubilization of membranes by detergents in *in-vitro* systems. One of ordinary skill

in the art in view of Draenert, would have no motivation to look prior art references dealing the solubilization of membranes by detergents in *in-vitro* systems. In fact, Draenert teaches away from such a combination in that Draenert is directed to an *in-vivo* process. It is readily apparent to one of ordinary skill in the art that a detergent delivered to or from the interior of the bone would result in cell lyses, which cell lyses could result in patient death.

Draenert does not teach or suggest removing bone marrow elements from the living bone of a patient to clean the bone and thereby produce a substantially cell-free bone matrix. Draenert does not teach or suggest solubilizing bone marrow elements. Rather, Draenert suggests only removing bone marrow in an amount sufficient to create a partial vacuum within the bone during arthroplastic surgery on a living patient. Draenert provides no motivation to look to prior art concerning *in-vitro* cleaning, solubilization of membranes, and/or detergents since Draenert is concerned with preserving the life of a patient during surgery. Draenert is not concerned with any of the problems encountered in cleaning cadaveric bones, *i.e.* thorough solubilization and removal of bone marrow elements. Draenert provides no motivation to look to art concerned with detergents and the use of detergents for solubilizing membranes (Helenius) and in fact teaches away from such a combination, since the delivery of detergents to the bone matrix in Draenert would result in cell lyses and patient death.

In view of the above, it is submitted that the combination of Draenert with Helenius is improper. It is noted that the board in *Ex parte Skinner*, 2 USPQ.2d 1788

(BPAI 1986) held that when the incentive to combine the teachings of the references is not immediately apparent, it is the duty of the Examiner to explain why the combinations of the teachings is proper.

c. *Assuming arguendo, the combination of Draenert with Helenius proper, the present claims are patentable and unobvious under 35 U.S.C. § 103, over Draenert in view of Helenius.*

Claims 59-69 are directed to a process for cleaning bone grafts. To establish a proper case of *prima facia* obviousness, the prior art as a whole must suggest the desirability of making the claimed combination and provide a reasonable expectation of success. Specifically, the prior art must suggest the desirability of the modification, *i.e.*, in the present case the prior art must suggest the desirability of delivering the detergent of Helenius to the interior of the bone using the method of Draenert, and must provide a reasonable expectation of success.

The present invention is directed to a process for cleaning large bone *grafts*. That is, a *cadaveric* bone (not a living bone in a patient) is selected and cleaned to remove bone marrow elements including any potentially biohazardous contamination including bacterial or viral contaminants. The produced cleaned bone graft is then suitable for transplantation into a living human patient. Draenert does not teach or suggest a process for cleaning a cadaveric bone so as to make it suitable for transplantation into a human. Rather, Draenert discloses removing bone marrow elements so as to create a partial vacuum for drawing bone cement into the honeycombs of the bone to firmly anchor an

implant in the bony bed during arthroplastic surgery on a *living* patient. Further, the present invention requires subjecting the cadaveric large substantially intact bone to a negative pressure-mediated flow of solvent. It is the solvent itself which is under negative pressure and is drawn through the bone to solubilize the bone marrow elements.

Contrary to the Examiner's assertion that it would have been obvious to one of ordinary skill in the art, at the time of the invention was made to include the detergents disclosed in Helenius and in the invention disclosed in Draenert in order to clean bone, Draenert does not teach or suggest delivering a detergent to or from the interior of a bone. In fact, Draenert teaches away from delivering a detergent to or from the interior of the bone, since such delivery would result in cell lyses which is hazardous to the life of the patient. Draenert is directed exclusively to an *in-vivo* method. Helenius is directed to the solubilization of membranes by detergents in *in-vitro* systems. It is well known to those of ordinary skill in the art that a detergent lyses cell membranes and is thus detrimental to a living system. Further, Helenius does not teach or suggest the use of detergents in an *in-vivo* system to any clean body tissue let alone cadaveric bone.

In the present case, Draenert requires that the method result in a living patient having a firmly anchored prosthesis. Draenert does not suggest desirability of modifying the method to deliver a detergent to the interior of the bone. Draenert does not suggest cleaning bone marrow from the bone. Rather, Draenert suggests removing an amount of bone marrow in order to create a partial vacuum within the bone. Draenert does not suggest cleaning bone, let alone cleaning bone by delivering a detergent to the interior of

the bone, since such delivery would result in cell lyses (cell death) and could result in the death of the patient. The combination of Draenert with Helenius does not provide a reasonable chance of success, since cleaning a bone using the detergent of Helenius to produce a cell-free matrix would result in patient death. Draenert teaches away from cell lyses since Draenert requires a living patient.

In conclusion, Draenert does not teach or suggest a process for cleaning a large bone graft by subjecting the bone to a negative pressure-mediated flow of solvent to solubilize the bone marrow. Further, Helenius does not overcome the deficiencies of Draenert, since Helenius also does not teach or suggest subjecting a large bone graft to a negative pressure-mediated flow of solvent to solubilize bone marrow elements, as required by the present claims.

In view of the above, Applicant asserts that Draenert constitutes non-analogous art. Assuming *arguendo*, Draenert constitutes analogous art, Applicant submits that the combination of Draenert with Helenius is improper. Assuming *arguendo*, the combination of Draenert and Helenius proper, it is submitted that the Examiner has not established a proper *prima facia* case of obviousness. It is submitted that neither Draenert nor Helenius, taken alone or together, suggest the present invention as claimed in claims 59-69. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

It is submitted that claims 59-69 are in condition for immediate allowance and early notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned attorney at the Stafford, Virginia telephone number on any questions that may arise.

Respectfully submitted,

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